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Market Round-up

V9 – 6th July, 2018

General Market News:

- ***Sanofi*** is focusing on driving a return to growth at its **diabetes** unit in the coming years and will consider acquisitions and partnerships to help boost performance.
https://www.channelnewsasia.com/news/health/sanofi-beefs-up-diabetes-pipeline-to-retrieve-success-10496156

- ***Amgen***, ***Novartis*** 'overwhelmed' by early interest in **migraine** drug **Aimovig**
https://www.fiercepharma.com/pharma/amgen-novartis-overwhelmed-by-early-interest-migraine-med-aimovig-expert

- ***Irish Pharmaceutical Healthcare Association*** calls for more State funding on medicines
https://www.irishtimes.com/business/health-pharma/pharma-body-calls-for-more-state-funding-on-medicines-1.3551487

- ***Novartis*** plans to spin off its ***Alcon*** eye care business to shareholders and buy back up to $5 billion in stock
https://www.bloomberg.com/news/articles/2018-06-29/novartis-to-spin-off-alcon-buy-back-up-to-5-billion-of-stock

- The ***HSE*** faces significant funding shortfall this year, PAC hears
https://www-irishtimes-com.cdn.ampproject.org/c/s/www.irishtimes.com/news/health/health-service-faces-significant-funding-shortfall-this-year-pac-hears-1.3555744?mode=amp

- ***MSD's*** antiviral **Prevymis** fails to win ***NICE*** backing
http://www.pharmatimes.com/news/msds_antiviral_prevymis_fails_to_win_nice_backing_1243303

Biosimilars/Biologics:

- ***Amgen*** announces top-line data from **Remicade** biosimilar study
https://www.nasdaq.com/article/amgen-announces-top-line-data-from-remicade-biosimilar-study-cm984753

- **ICER** gives thumbs up with caveats for ***Novartis*** and ***Amgen's*** novel **migraine biologic**
https://www.thepharmaletter.com/article/icer-gives-thumbs-up-with-caveats-for-novartis-and-amgen-s-novel-migraine-biologic

Drug Approvals:

- ***Pfizer*** announces **XELJANZ** received European marketing authorisation for active Psoriatic Arthritis
https://www.streetinsider.com/Corporate+News/Pfizer+%28PFE%29+Announces+XELJANZ+Received+Marketing+Authorisation+in+EU+for+Active+Psoriatic+Arthritis/14354759.html

- ***GSK's*** **Bexsero** vaccine has received European approval for lower dose of their **Meningitis** vaccine
https://www.pharmaceutical-technology.com/news/gsk-secures-european-nod-lower-dosing-

option-meningitis-b-vaccine/

Further Reading:

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- Paschal Donohoe links Government funding to ***HSE*** reforms
  Drugs companies are rising to the challenges of research into superbugs
  https://www.irishtimes.com/news/politics/paschal-donohoe-links-government-funding-to-hse-reforms-1.3546952

- The **World Health Organisation** in collaboration with ***Ferring*** and ***MSD for Mothers***, has found a cure for **Post-Partum Haemorrhage**
  https://www.thisdaylive.com/index.php/2018/07/05/who-announces-cure-for-excessive-bleeding-after-childbirth/

- Is ***Pfizer's*** price hike an effect of drug policy on sector?
  https://www.nasdaq.com/article/is-pfizers-price-hike-an-effect-of-drug-policy-on-sector-cm986983

- ***Pfizer*** raises prices of 40 drugs despite US President's prediction for lower drug prices
  http://www.pharmabiz.com/NewsDetails.aspx?aid=109825&sid=2

- ***Shire*** partners with Arianna Huffington to encourage 'Screen Responsibility'
  https://www.mediapost.com/publications/article/321597/shire-partners-with-arianna-huffington-to-encourag.html

Long Read

- **Cancer treatments that mobilise the sufferer's immune system to fight the disease have dramatically altered the odds for some patients in recent years. But who will be able to access them –and at what cost to the state?**
  - *Article published in BusinessPost, July 1st, by Susan Mitchell.*

Jessica Grehan has stage four lung cancer. She has been asking Minister for Health Simon Harris for access to immunotherapy drugs since the middle of 2016.

So far, Harris has refused to budge. "He said he was unable to influence the HSE's decision-making," said Grehan.

One of the drugs Grehan is anxious to try is called **Keytruda**, or **Pembrolizumab** (Pembro).

Pembro is one of a handful of promising treatments that unleashes a person's own immune system to attack cancer cells. These immunotherapy drugs have been making steady gains against a number of cancers.

In Europe, **Pembro** is authorised for the treatment of various cancers including melanoma and non-small cell lung cancer (the most common type of lung cancer), as well as classical Hodgkin lymphoma and urothelial cancer (a cancer of the bladder and urinary tract) that is advanced or has spread to other parts of the body.

The Irish health service is covering the cost of **Pembro** for patients with melanoma and the most common type of lung cancer – although it has restricted its use (more details below).

Although she has lung cancer, Grehan does not meet the specific criteria.

The government has decided to facilitate early access to the drug for women affected by the recent CervicalCheck debacle, raising obvious questions on whether political expediency is trumping equity of access.

Should certain patients with cancer be given preferential treatment ahead of others?

The government made this announcement even though Pembro is not yet approved (by the European Medicines Agency) to treat cervical cancer in Europe.

“I was gobsmacked. I am at a loss as to how [Simon Harris] can say he can’t do anything for me and yet he can for them,” said Grehan. “This is one of the very few options I have left. I’d really like to know how some people can get access to it, yet others are being denied. There is no transparency around the process.”

So what exactly has the minister promised to the women affected by the CervicalCheck crisis?

In a statement, the Department of Health said: “The government has agreed to put in place a comprehensive package of support for women (and their families) affected by the recent CervicalCheck issues.”

It said the package included the refunding of out-of-pocket medical expenses,“ including the cost of any medicines which have been prescribed by their treating clinicians and which may or may not be covered by their medical card or private health insurance should they have such a policy, and including medicines which may not be approved for reimbursement, once prescribed by their treating clinician”.

The department said that while the government decision did not reference any particular medicine or drug, it was “correct to say that Pembro would be included and that the costs of the drug would be met by the HSE as part of the support package, as long as it was prescribed by a woman’s treating clinician”.

The department was unable to guarantee that other women with cervical cancer would be able to access experimental treatments but said this was being explored.

Oncologists warned this created obvious problems regarding equity of access for patients with cervical cancer: the message being that you must have received a false negative smear test in order to have the drug funded by the state.

“There is an obvious equity issue,” said consultant oncologist ***Dr David Fennelly.***

Immunotherapies and effectiveness

Immunotherapies have dramatically altered the odds for some of the sickest patients since they were introduced in recent years.

At the recent annual meeting of the American Society of Clinical Oncology in Chicago, the world’s largest cancer conference, doctors hailed immunotherapies as the biggest advance in tackling the disease for decades. They have now been approved for use in a long list of cancers.

One of the main types of immunotherapy involves prescribing immune checkpoint inhibitors. These drugs basically take the breaks off the immune system. Pembro targets PD-L1, which is a protein found on cells in the body. It normally acts as a type of ‘off switch’ that prevents immune cells from attacking cancer cells. Some cancer cells have large amounts of PD-L1, which helps them hide from immune attack.

Pembro is used to treat various cancers, including non-small cell lung cancer, advanced melanoma, head and neck squamous cell cancer and advanced ur othelial bladder cancer.

Pembro is manufactured by Merck (also called MSD). The consultancy firm EvaluatePharma has predicted that by 2024 Pembro will be the top-selling orphan drug in the world, notching up sales of €12.7 billion.

In June, Merck unveiled a late-stage study of almost 1,300 patients that showed Pembro boosted survival in patients with non-small cell lung cancer.

Patients taking the drug lived for an average of 16.7 months verses 12.1 months on chemotherapy, although those whose tumours contained higher levels of PD-L1 did substantially better.

In Ireland, the HSE will only reimburse the cost of Pembro for the most common type of lung cancer in patients whose tumours express PD-L1 with "a ≥50 per cent tumour proportion score".

Grehan does not have enough of that protein, so she cannot access it.

However, clinical trial data shows that those whose tumours express lower levels of the protein can also benefit.

"The rules are too restrictive," said consultant oncologist ***Professor John Crown***, who believes more patients with lung cancer should be allowed to access Pembro. According to a study published in the Journal of Clinical Oncology, Pembro may actually cure a subset of patients with metastatic melanoma.

Last month, the US Food and Drug Administration (FDA) expanded the approval of Pembro for the treatment of patients with recurrent or metastatic cervical cancer. Cervical cancer patients previously had few treatment options other than toxic chemotherapy.

Vicky Phelan, whose story about CervicalCheck triggered a cascade of revelations and resignations, has been publicly advocating for better access to immunotherapies such as Pembro for patients with cervical cancer and other cancers. Phelan is getting Pembro. She recently spoke about the positive impact the drug is having on her cancer, saying there had been significant shrinkage in her tumours.

So are we talking about a new wonder drug for patients with advanced cervical cancer?

The FDA approval was based on a trial which enrolled 98 patients. This is a small sample. Among those patients, 77 had tumours that expressed PD-L1. The response rate was 14.3 per cent, with a complete response rate of 2.6 per cent and partial response rate of 11.7 per cent.

Professor Michael Barry, who heads up the medicines watchdog, the National Centre for Pharmacoeconomics (NCPE), said the clinical trial data was "not that impressive and [was] relatively immature".

Barry said that responses were predominantly based on CT scans. Some showed a partial response, meaning their tumours had diminished in size by 30 per cent or more.

A complete response means that there was no evidence of the disease, suggesting that this could in fact prove to be a cure for some patients.

Might it be a cure?

"Possibly," said Barry.

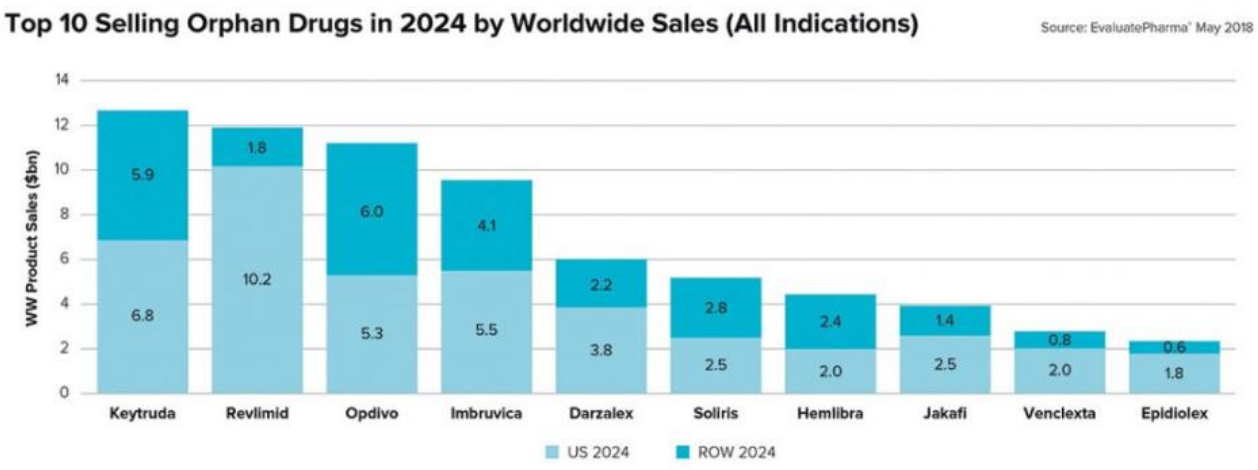
"Do I think it is? Absolutely not. It is slowing it down, but it is important to say that does not mean it will prolong life."

Fennelly is treating Vicky Phelan and others with cevical cancer. He was a lot more positive.

"The potential is very exciting. There is no doubt that the responses I have seen are responses you just do not see with chemotherapy," said Fennelly.

"We have a signal that there could be something there, but it is still in its infancy," said ***Professor Donal Brennan***, who specialises in gynaecological oncology.

Brennan said it was also clear that in patients who did respond, the response was "durable" – or long-lasting. "That is different to what we have seen before."



Brennan cautioned that Merck had only done an early trial. He said many drugs fail in Phase 3, when they are compared to the existing standard of care. He cited a study on the estimation of clinical trial success rates between 2000 and 2015. It concluded the overall probability of success – moving from Phase 1 to eventual approval – was 14 per cent across all indications (infectious diseases and all other conditions), but, at 3.4 per cent, it was considerably lower for oncology.

Simon Harris has asked the HSE and the Department of Health to develop a clinical trial structure to enable patients with advanced cervical cancer to get early access to Pembro.

Barry said the state appeared to be on the cusp of funding a trial for the manufacturer. He said this was “unprecedented – at least in Ireland”.

“This costs €116,000 per year at the list price. We have negotiated discounts off that list price for use of the drug in other indications,” said Barry, who questioned whether we would get a reduced price for its use in patients with cervical cancer.

Fennelly estimated that about 60 patients affected by CervicalCheck could be eligible for a future trial. That would cost €7 million per year.

Fennelly said that – outside of the CervicalCheck cohort – approximately 50 women per year could benefit from accessing a future trial.

That would bring the total cost to €13 million per year, Barry said.

Barry recommended a risk-sharing agreement, which is “where the state only pays the manufacturer for those who respond and not for others.

“It would be a much more prudent use of scarce resources,” he said.